60. On Jan. 26, 1998, Anne M. Reb NP, a Regulatory Review Officer of the Dept. of Health & Human Services ("DHS"), Division of Drug Marketing, Advertising and Communications ("DDMAC") sent a letter via fax to BMS's VP & Senior Counsel, Thomas E. Costa. This untitled letter was in regard to: NDA 19-898, Pravachol (pravastatin sodium) tablets, MACMIS ID # 5878. Ms. Reb notes in this letter communications made to a DDMAC representative by a BMS sales representative at the 1997 American Heart Association ("AHA") meeting. The letter notes that "DDMAC has reviewed these materials and communications and has determined that they are misleading in violation of the Federal, Food, Drug, and Cosmetic Act and applicable regulations" for the following reasons:

a. The BMS sales rep, Paul Spence discussed mechanisms of action for Pravachol that are not consistent with the approved product labeling.

b. The rep discussed the reanalysis of the WOSCOP study and stated that the reduction of first MI with Pravachol is related to mechanisms of action other than LDL-C lowering.

c. The BMS rep also provided promotional materials citing information supporting this claim. For example, the rep cited a passage in the reprint "Reduction in Cardiovascular Events During Pravastatin Therapy" by Byington et al., (1995) that discusses alternative mechanisms of action other than LDL-C lowering. Specifically: "This finding suggests that this agent (Pravastatin) may have an effect beyond simple lipid lowering. Mechanisms such as plaque stabilization, restoration of endothelial function, and a decrease in platelet activation are possible explanations for this additional benefit."

d. The BMS rep also referred the DDMAC rep to a BMS sponsored continuing medical education symposium on Nov. 9 and 11, 1997, for further discussion of this issue.

e. The DDMAC letter notes that this promotion is misleading because it is not consistent with the mechanism of action provided in the approved product labeling for Pravachol.

f. DDMAC's letter clearly points out that the product label states "the effects of pravastatin on Lp(a), fibrinogen, and certain other independent biochemical risk markers for coronary heart disease are unknown."

g. Page 4 of the DDMAC letter reviews the use of the "Reanalysis of the WOSCOP Study", which was published in the journal Circulation, April 21, 1998. BMS was using the information from this study, prior to publication in their promotional brochures. This paper within BMS was commonly known as the "Quintile Anaylsis".

h. DDMAC notes in their letter that this data is misleading because the trial was not designed to test for differences in outcome (MI Events) based on percent LDL-C reduction. The paper was not a prospective study, but a post-hoc analysis of the data. DDMAC notes the conclusions are misleading.

i. DDMAC further notes that the BMS promotional information is misleading because it is not consistent with the National Cholesterol Education Program's (NCEP) Treatment Guidelines.

j. DDMAC also notes that indeed the NCEP guidelines are treatment goals and lowering LDL-C below these goals, if possible, is desirable.

k. Pages 5-6 of the DDMAC letter goes into some detail about the misleading presentation of mechanisms of action by the BMS promotional material. The claims by BMS were not consistent with the approved product label and BMS was implying that reduction of first MI was related to mechanisms other than LDL lowering.

l. DDMAC concludes that "Thus, it is misleading to imply that the reduction of first MI with Pravachol in the WOSCOP study is related to mechanisms of action other than LDL-C or lipid-lowering because the data are not adequate to support the clinical significance of this claim."

m. DDMAC requests that BMS immediately discontinue the dissemination and use of the violative pieces noted in this letter and any other promotional materials that contain similar themes. They also request a response from BMS no later than Feb 9, 1997 [should be 1998, typo in letter]. The requested response should include a list of misleading promotional activities and materials discontinued. DDMAC also asks for a plan to comply with their request.

61. As the DDMAC letter dated January 26, 1998 to BMS shows, as early as 1997, BMS was documented using misleading reprints, data and other resources to promote that Pravachol had unique, secondary mechanisms of action that were responsible for CV event reduction. This was off-label and is still not within the approved labeling of Pravachol today. Although BMS was told to discontinue and not use those misleading reprints and other off-label information to promote Pravachol as early as January of 1998, as documented by the Relator BMS continued to do so until some point in 2003. The

misleading information and reprints used by BMS has never been within the approved labeling of Pravachol and remains off-label today.

62. The National Heart Lung and Blood Institute's (NHLBI), National Cholesterol Education Program's (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III (ATP III)) had added new intensity to LDL-C lowering in patients with multiple Coronary Heart Disease (CHD) risk factors about 2000 or 2001. This change put Pravachol at a market disadvantage to more potent cholesterol lowering agents. The changes advocated more aggressive lowering of LDL-C. Since pravastatin had more moderate LDL-C lowering ability than other statins, notably atorvastatin (Lipitor) and simvastatin (Zocor), the market share for pravastatin was declining in many markets across the country.

63. It became clear to the field sales force, home office sales and marketing departments and medical department that there was a clear opportunity to sell Pravachol using the off-label mechanism of action promotional message. It clearly had impact on keeping Pravachol loyalists to continue prescribing the drug and those doctors who were not big prescribers to use more Pravachol due to this message. This off-label marketing strategy was implemented by BMS on a nation-wide basis to sell Pravachol using this off-label mechanism of action promotional message.

64. In response to these market factors, especially the physician and national guideline supported thought that "lower LDL-C was better", in 1999 Bristol-Myers Squibb (BMS) formed a special promotional force called Medical Science Associates (MSA). These sales representatives were under the direct authority of the BMS Medical Department and focused solely on Pravachol promotion. Steve Noyes, a former employee and VP with

BMS was directly involved with the formation of the "quasi-medical" team. The representatives that were hired into this force of 'quasi-medical' people did not require, and most did not have, any official degree or certification in pharmacy, life sciences or other medically related field.

65. About 140 MSA positions were created nationwide. The people that were hired for this team came primarily from the field sales representative position, although they did interview people from outside the company. This team was focused on the promotion of Pravachol.

66. The MSAs were in addition to the real medical team of Medical Science Managers ("MSM"), which are now called Medical Science Liaisons ("MSL"). The people hired for these MSM/MSL positions are actual medical personnel, usually PharmDs. The MSAs were used to supplement the real medical team with sales/medical individuals that would do 1-on-1 and evening presentations to physicians under the guise of being "medical" personnel.

67. The MSAs were provided with Power Point slide decks that contained off label information to present to physicians as Science liaisons- not sales people with BMS in order to influence prescribing behavior.

68. These slide decks involved presenting information on Pravachol's action as an anti-thrombotic, and its effect on hsCRP, Interluekin-6, CD-40 ligand, etc., and Pravachol's 'potential' effect on these risk factors – all of which were not in the FDA approved labeling for Pravachol.

69. The MSA sales force was in operation until approximately mid 2000, when it was dissolved and the MSAs were transitioned into CMRS (Cardiovascular Metabolic Risk

Specialists) representatives. The relator was a district manager of the newly formed CMRS team. The MSA sales force was formed to promote various off-label claims for Pravachol that still do not exist in its approved FDA labeling, either as indications, clinical pharmacology or other aspects of the prescribing information. These off-label claims used by BMS to promote Pravachol were identical to those BMS claims set forth in the DDMAC letter of January 26, 1998 that the FDA stated were misleading.

70. The off-label promotional tactics that were employed by the MSA sales force was transferred to the CMRS sales force and BMS knowingly continued the off-label promotion of Pravachol on a nationwide basis through the CMRS sales force. This promotional sales force was provided with Medical power point slide decks with off-label claims (both MSA slide decks and they routinely shared the medical slide decks of the Medical Science Managers (MSM)) to use in proactive one on one promotion of these claims for Pravachol to a broad panel of health care providers, not in response to unsolicited requests.

71. In a MSA Business Plan prepared by Richard Yunger, an MSA, for the end of 2000 to early 2001 time frame, several improper tactics and objectives for MSAs were documented for the top 21 targeted and ranked physicians, including doctors whose patients were enrolled in either Medicare or Medicaid. For example, in order to "consistently build prescription share" the following tactics were implemented: DAB member, CACs, Region Fly-To Programs, charitable support, possible Golf Programs. Other tactics documented included "Pull through Rx share as a result of CAC attendance and Fly-To attendance" and "2002 Fly-To" and utilizing the "fax back program." Additionally, the MSA "Powerpoint presentation" was listed as a specific tactic.

72. During the existence of the MSAs from 1999-2000, the MSAs were direct reports within the BMS corporate structure of the RADs (Region Area Directors of the Medical Department). So the MSAs were under the direct authority of the Medical Department, not the sales department. To the relator's knowledge, this was a significant conflict, as the two departments, Sales and Medical should have had a clear firewall between them in regard to product promotional efforts (sales) versus product medical informational efforts (medical).

73 Relator was a hospital District Business Manager (DBM) in Florida/Georgia at the time and was transferred over to be a DBM for the newly formed CMRS sales force of Florida/Georgia/SC in August of 2000, so all of the relator's reps were former MSAs.

74 The market dynamics during these years were as follows. Zocor and Lipitor had shown greater reductions in LDL Cholesterol and total Cholesterol when compared to Pravachol. Although Pravachol had indications for reducing Cardio-Vascular ("CV") events in certain patient types, the medical community in general was moving to a "lower is better" philosophy concerning LDL & total cholesterol. This mindset put Pravachol at a disadvantage in the market place, even with its indications to reduce CV events. Providers were prescribing increasing amounts of the more potent agents of Zocor and Lipitor and taking market share or New RX growth away from Pravachol.

75. BMS's deliberate off-label strategy with the MSAs was to sell providers that Pravachol reduced events by unique off-label 'other mechanisms' rather than merely lowering LDL and total cholesterol. Therefore, BMS designed a promotion based on off-label information to argue that Pravachol was a better treatment choice for patients at risk of CV events than the more potent cholesterol reducing agents.

76. When the MSAs moved into the CMRS position, this off-label approach to selling Pravachol continued not just with the CMRS sales force but also spread to the primary care sales force (PSR), and BMS's paid speakers and consultant physicians were delivering the same off-label message. Initially the CMRS were also provided Power Point slide decks to use with some of the same off-label information and strategies in them.

77. BMS relied on off-label information contained in scientific papers when carrying out this off-label promotion scheme. These off-label promotional tactics were used and implemented nationwide by BMS with full knowledge of both BMS sales and BMS medical management. They were shared at BMS National Plan of Action meetings (POAs), in best practice sharing sessions, district level meetings and inter-regional teleconferences and best practice sharing sessions.

78. As part of this off-label promotion, the BMS sales force tried to show that competitive cholesterol lowering agents produced by other companies had little or no effect on CV events and these "other mechanisms," even though they reduced both total and LDL cholesterol. BMS knowingly promoted in a misleading manner by stating that Pravachol reduced events by off-label "other mechanisms," often shown to be unique to Pravachol, for the purpose of causing or getting a false or fraudulent claim paid or approved by the Government.

79. The term "other mechanisms" can be used interchangeably with "non-lipid lowering effects", "ancillary mechanisms", "alternative mechanisms", "pleiotropic mechanisms" (pleiotrophy as used with cholesterol agents is not the traditional definition of describing a genetic effect of a single gene on multiple phenotypic traits. In regard to it's use with

cholesterol agents the term has been changed to 'statin pleiotrophy' which encompasses all of the non-LDL mediated effects of statin therapy). (Cholesterol agents, Zocor (simvastatin), Lipitor (atorvastatin), Pravachol (pravastatin), Mevacor (lovastatin) & Lescol (fluvastatin) are commonly referred to as 'statins').

80. The papers and other documents used by BMS in this off-label promotion scheme list the following off-label 'other mechanisms' that were attributed to Pravachol and used in the off-label promotion of Pravachol. These 'other mechanisms' were presented as a major reason Pravachol should be prescribed over other drugs of this class. The list of off-label "other mechanisms" that was used include, but are not limited to, the following:

- independent effect on endothelial function
- independent effect on platelet function
- differential effect on smooth muscle cell proliferation vs other statins
- Pravachol's effect on plaque pathophysiology
- Plaque physiology
- Plaque stabilization
- Inflammation
- Pravachol's anti-thrombotic properties vs Mevacor, Lipitor and Zocor's prothrombotic properties
- Effect on fibrinogen levels
- Effect on Factor VII
- Effect on PAI-1 levels
- Effect on endothelial vasodilation
- Effect on blood viscosity
- Effect on LDL oxidation
- Effect on platelet deposition
- Effect on macrophage number and cholesterol ester accumulation
- Effect on platelet aggregation
- Endothelial normalization
- Anti-inflammatory effects
- Depletion and physicochemical stability of lipid core
- Strengthening of fibrous cap
- Inhibition of platelet thrombus formation and deposition
- Reduction of thrombogenic response
- Plasma viscosity decreased
- Anti-atherothrombotic effects
- Hematorheologic effects

- Decreased platelet thrombus formation at both high and low shear rates vs Zocor's effects
- Decreased mural thrombus formation
- Decreased lipid content of plaques
- Improvement in vascular reactivity
- Reduce the number of inflammatory cells
- Effect on matrix metalloproteinases
- Effect on CD-40 ligand

81. BMS specifically targeted all of the doctors and medical providers, and also targeted specific key (high volume) prescribers, with this off-label message during the relevant time frame.

82. The CMRS and also the PSR sales forces focused a high level of activity and resources on big Medicaid (nation wide) and Medicare (in Florida) prescribing physicians. This segment of providers offered the single largest open formulary in most states for Pravachol sales. Pravachol had hundreds of millions of dollars in sales every year from 1998- 2003, the years of this intense off-label promotional scheme. BMS knew that this promotion was saving them from losing market share as rapidly as the "lower is better" mindset was causing.

83. BMS routinely promoted its trial, TIMI-22 or PROVE-IT, which was unpublished at that time (2000-2003), and used it as bait to keep healthcare providers 'on the hook', as a reason to prescribe Pravachol and continue to prescribe it, stating that PROVE-IT would upon conclusion, prove that these claims made about Pravachol's affects on ancillary mechanisms of action for event reduction were true. BMS knew that by using this off-label promotion and talking up the Prove-It trial for years before publication to string doctors along and that it was keeping a lot of patients on Pravachol, just because BMS was doing the study. BMS marketing and sales administration people commonly said, to the effect, "it doesn't matter what the results are, it's keeping doctors writing Pravachol."

84. BMS purposefully used these slide decks and unapproved, reprints, abstracts, letters and poster session abstracts to make proactive unapproved off-label claims for Pravachol. BMS deliberately misled healthcare providers by selectively highlighting, emphasizing and promoting claims for which Pravachol had no approved indication. BMS routinely made invalid comparisons between various product studies to selectively make positive claims for Pravachol and negative, deliberately misleading and even injurious, claims about other statins produced by competitors, even though some other statins had FDA approved indications to reduce CV events.

85. Many of the studies that were used in the off-label promotion of Pravachol were lab and animal studies (such as studies on rat cells, dog cells and pig arteries), they were not even done in humans. Some were not even published at the time of their use in slide decks.

86 In their use of these unapproved reprints, there was not approved FDA prescribing information attached, and the unapproved claims were routinely woven into promotional sales calls with no statement, markings or other delineation that these unapproved claims were not in the approved FDA labeling for Pravachol.

87. This off-label marketing strategy was specifically developed by BMS, to address the cholesterol market changes that put Pravachol at a marketing disadvantage relative to more potent cholesterol lowering agents, without regard for patient safety, and BMS intended that this off-label promotion to cause physicians to submit false claims for payment by the United States and the various states through government reimbursement programs.

88. Upon dissolution of the MSA sales force in 2000, the tactics and methods of their off-label promotion continued unabated by the CMRS, PSR sales forces, BMS paid speakers

and the BMS medical department through MSMs until approximately 2003, with full knowledge and encouragement of BMS management.

89. BMS purposely mixed its on label promotional efforts of Pravachol with proactive medical unapproved claims. This was done via a nationwide plan in order to manipulate the data of the clinical impact of Pravachol's mechanisms of action in preventing CV events and efficacy compared to other cholesterol lowering agents. BMS implemented this misleading off-label promotion strategy even in light of national guidelines that were advocating more aggressive cholesterol reductions and proactively used the PROVE-IT trial for years before its publication, to string providers along with the promise of proving Pravachol's unapproved affects were the primary factors involved in CV event reduction. BMS undertook this strategy from 1999 – 2003 to the majority of cardiologists and all other relevant specialties involved with lipid control, especially high volume Medicaid doctors. These practices were developed, shared, trained, encouraged, set forth as expectations to sales representatives and Medical Science Managers. BMS orchestrated this strategy ignoring the adverse impact on public health and safety in order to boost and maintain sales of Pravachol.

90. In fact, the entire promotional and sales message was intended by BMS to mislead the listener to believe that in regards to cholesterol and CV event reduction, "LOWER IS NOT BETTER," which directly contradicted the NCEP treatment guidelines, and intended to cause the submission of false claims for payment for prescriptions of Pravachol based on this off-label promotional campaign. This was done overtly and subtly. For example, many of the studies and other statements made in promoting Pravachol were misleading by pointing to data to make the "lower is not better" case.

However, the paper cited in the ZAP Plan, "Hydrophobic vs. Hydrophilic statins article: (Lancet Vol 359, June 22, 2002;2195-98)", makes several statements that the other statins actually had detrimental effects on CV event prevention, even though they reduced cholesterol more than Pravachol and some had FDA approved indications for CV event reduction. This claim by BMS was deliberately misleading when made, but it was also proven to be false when the results of the PROVE-IT trial were ultimately published.

B. Use of PROVE-IT Study to Mislead Doctors and Reinforce BMS's Off-Label Promotion and Misbranding of Pravachol And Resultant Harm to Patients.

91. BMS assisted in and sponsored a study called the PROVE-IT study that was designed to document intensive versus moderate lipid lowering with statins after acute coronary syndromes. In essence, the PROVE-IT study compared the effectiveness on CV events of two drugs, Pravachol, produced by BMS, and Lipitor produced by Pfizer.

92. Patients were enrolled in the PROVE-IT study between November 15, 2000 and December 22, 2001.

93. During the course of the PROVE-IT study trial BMS used the study design and potential results to reinforce BMS's off-label and misleading claims that Pravachol's unique mechanistic actions, instead of its cholesterol lowering ability, were responsible for CV event reduction. For example, BMS used a Slide deck that contained a slide entitled "Lipids in Coronary Artery Disease (L-CAD) Study Design," which was supplied to the CMRS sales force to use in one on one presentations to providers in 2002. The purpose of this slide deck was designed to introduce the PROVE-IT trial as giving the final answer to the question; is lower better? BMS's strategy was for the PROVE-IT study to buy time with doctors by saying, lower isn't necessarily better for CV event reduction, and BMS won't know until Prove-It is finished and published. This was critical to setting

up the argument that "other mechanisms" were responsible for Pravachol's effects on CV event reduction. "PROVE-IT will show that is true," was the standard response to doctors who questioned the use of Pravachol in light of the "lower is better" consensus following the publication of the national guidelines (ATP III). The Slide Deck notes that one of the goals was "Mechanistic sub studies to understand complexity of ACS." ACS is Acute Coronary Syndrome, which includes myocardial infarction ("MI") and unstable angina. Additionally, a key slide in this Slide deck explained the design of PROVE-IT, by stating:

- "Available data suggest that extremely aggressive LDL-C lowering may not result in significantly greater clinical event reduction"
- "Different effects on other lipids and alternative mechanisms may affect clinical benefit seen between agents"
- The notes section explains how "pleotropic mechanisms may play as role in the efficacy of each drug." The notes also state the study is "to determine the contribution of alternative mechanisms of the specific statin."
- The notes also speak to atorvastatin having greater LDL-C lowering ability, but that alone cannot support more clinical event reduction.

94. On March 8, 2004, the results of the PROVE-IT study were publicly released and on April 8, 2004 the New England Journal of Medicine published the "TIMI-22" or "PROVE-IT" study. The official title in the journal was "Intensive versus Moderate Lipid Lowering with Statins after Acute Coronary Syndromes," by C. Cannon M.D., et al.

95. The study involved a total of 4162 patients treated with either 40mg pravastatin (Pravachol) or 80mg atorvastatin (Lipitor).

96. Kaplan-Meier estimates showed that patients treated with atorvastatin (or Lipitor) (a more aggressive LDL-C lowering regimen) for a mean of 24 months had an event rate of the primary endpoint of 22.4% versus 26.3% in the pravastatin (or Pravachol) treated

group, reflecting a statistically significant 16% reduction in the hazard ratio in favor of atorvastatin (Lipitor) (P=0.005; 95 percent confidence interval, 5 to 26 percent).

97. The PROVE-IT study showed that for every 4162 patients treated an average of 24 months the pravastatin (Pravachol) patient group suffered 73 more events than the atorvastatin (Lipitor) treated group. The primary endpoint was a composite of death from any cause, myocardial infarction, documented unstable angina requiring hospitalization, revascularization (performed at least 30 days after randomization), and stroke.

98. The results of the PROVE-IT study were the opposite of claims made by BMS to physicians through the off-label promotion marketing scheme for Pravachol.

99. The market share data for Pravachol before and after the PROVE-IT results clearly show that the "lower is better" fact had a significantly detrimental affect on Pravachol market share. There was a drastic decline in the market share of Pravachol following the release of the PROVE-IT study.

100. Prior to embarking on the PROVE-IT study, BMS knew this would be the result of the "lower is better" message if left unchallenged. The off-label Pravachol promotion was the company's best answer to this market reality and BMS deliberately misled its customers into believing that lower cholesterol was not better and used the PROVE-IT study to reinforce BMS's off-label promotion of Pravachol.

101. The result of these misleading promotional claims by BMS is that many thousands of patients between 1999 and 2003 were prescribed Pravachol inappropriately, which was paid for by various U.S. Federal healthcare programs. Furthermore, the PROVE-IT trial upon publication showed that for every 4162 patients, there were 464 CV events in the Lipitor treated group versus 537 CV events in the Pravachol treated group. This resulted

in an absolute difference of 73 (or approximately 17.5%) more CV events in less aggressively treated Pravachol patients. These promotional tactics were pursued by BMS for sales dollars, but resulted in thousands of patients having higher risks of, or actual higher rates of CV events, including MI, angioplasty, CABG, stroke or death.

C. Use of Reprints, Abstracts, Etc. to Disseminate Off-Label and Misleading Information.

102. BMS used unapproved reprints, abstracts, letters and poster session abstracts containing off-label information, including off-label information that BMS was expressly warned by DDMAC not to use because they were misleading and contained off-label information. Nonetheless, BMS used these reprints and other off-label information to make proactive unapproved off-label claims for Pravachol. This aggressive off-label promotion by BMS continued for years after the DDMAC January 1998 letter was sent to BMS. Reprints containing off-label and misleading information were routinely used by all medical and sales representatives at the direction of BMS across the nation for off-label promotion of Pravachol.

103. One reprint containing off-label information that BMS continued to use to promote Pravachol was the reprint entitled, "Influence of Pravastatin and Plasma Lipids on Clinical Events in the West of Scotland Coronary Prevention Study (WOSCOPS), Circulation, April 21, 1998. This reprint was also known as the "Quintile Analysis" within BMS, and it was expressly referenced in the DDMAC letter of January 26, 1998 as containing misleading information that was off-label.

104. This WOSCOPS reanalysis paper was routinely used by BMS, its paid speakers, Medical Science Managers (MSM), Medical Science Associates (MSA), Cardiovascular Metabolic Risk Specialists (CMRS) and Primary Care Representatives (PSR) for years

after the DDMAC letter of January 26, 1998 as a promotional resource in selling to individual physicians. It was used by BMS speakers, both external and internal, taught to BMS sales reps and routinely used across the nation in promotion of off label mechanisms for reduction of serious CV events (notably MI, CV procedures of angioplasty and coronary by-pass, stroke and death.

105. The January 26, 1998 DDMAC letter also references the reprint, "Reduction in Cardiovascular Events During Pravastatin Therapy" by Byington et al., (1995) also being used in misleading off-label promotion of Pravachol. This reprint was also routinely used by BMS, its paid speakers, Medical Science Managers (MSM), Medical Science Associates (MSA), Cardiovascular Metabolic Risk Specialists (CMRS) and Primary Care Representatives (PSR) for years after the DDMAC letter of January 26, 1998 as a promotional resource in selling to individual physicians.

106. The Byington study contained off-label information that DDMAC told BMS was misleading and should not be used to promote Pravachol, specifically: "This finding suggests that this agent may have an effect beyond simple lipid lowering. Mechanisms such as plaque stabilization, restoration of endothelial function, and a decrease in platelet activation are possible explanations for this additional benefit."

107. Additionally, the Byington study contained other off-label and misleading information that should not be used, including the statement: "This suggests that whereas pravastatin exerts at least some of its effect on MI reduction through its effect on LDL cholesterol reduction, the clinical effect also may result in part from some ancillary property of the drug."

108. BMS used these reprints containing misleading and off-label information as tools to promote Pravachol. For example, as documented in an email from Brett Steckman (a PSR rep and PharmD.) a few years after the DDMAC letter of January 26, 1998, one of BMS's paid speakers, Dr. John Steinberg, continued to disseminate off-label information as well as information from the WOSCOPS reanalysis reprint and the Byington paper to PSR reps in the Baltimore area to assist BMS sales reps to sell Pravachol. Ms. Steckman observed that Dr. Steinberg made the following points:

- "Pravachol is an IMPRESSIVE anti-thrombotic drug. Compare Pravachol's anti-thrombotic properties to some of Mevacor, Lipitor, and Zocor's prothrombotic properties and one can see how negative properties can offset impressive lipid lowering status."
- "LOWER IS NOT BETTER"
- "LOWER IS NOT NECESSARILY BETTER" and states the relationship between event reduction and cholesterol reduction is not linear.

109. The information conveyed by Dr. Steinberg to BMS sales reps was used by BMS to clearly encouraged BMS representatives to develop an off-label sales strategy based on the "other mechanism" argument and this off-label data and strategy was used nationwide by BMS field sales, medical and management teams.

110. In or about mid-2002, BMS developed what was referred to as the Pravachol Zocor Attach Plan, or ZAP Plan, which was a 45-day plan of attack to compete with Zocor. The ZAP Plan was instituted because of a label change for Zocor that put tighter restrictions on Zocor dosing with some other drugs. Pravachol did not have those same restrictions, therefore, this was a market event to take advantage of by BMS. However, the misleading promotion of off-label other mechanisms continued throughout and was incorporated into

the ZAP Plan. The ZAP Plan was implemented in the West Area of the country, from the Mississippi River to Hawaii.

111. The ZAP Plan lists Faxbacks as resources to promote Pravachol, including Faxback Prav02 Alternative MOA (mechanism of action), and Faxback Prav04 LDL-C Red[uction] vs. CV Event Red[uction], and BMS routinely used this tactic proactively to get off-label information to prescribers in deliberate violation of the rules governing the use of Faxbacks.

112. The ZAP Plan lists several reprints that directly promote the misleading and off-label information about "other mechanisms" in Pravachol being the reason for CV event reduction, instead of LDL-C reduction. For example, the ZAP Plan referred to a reprint containing off-label and misleading information entitled, "Effects of pravastatin on mortality in patients with and without coronary heart disease across a broad range of cholesterol levels," by J. Simes, et. al (Known in BMS as the PPP or Pravastatin Pooling Project study).

113. Additionally, the ZAP Plan recommended two other reprints that contained off-label and misleading information to attack Zocor: (1) Katholi "If LDL-C Is the Answer…What was the Question?" (Heart Disease, 2001 Vol. 3 No 1; 2-13), which includes statements that were used to promote the misleading idea of other mechanisms in Pravachol being responsible for CV event reduction, and that many if not most of these mechanisms were unique to Pravachol among the statin drug class; (2) "Disparity between angiographic regression and clinical event rates with hydrophobic statins," (Known as the "Hydrophobic vs. Hydrophilic statins article") (Lancet Vol 359, June 22, 2002; 2195-98), which makes the misleading point that Pravachol offered some unique mechanism of

action versus the other statins in CV event reduction and actually makes overtly misleading statements that the other statins (which are hydrophobic vs Pravachol which is hydrophilic) have detrimental effects on CV event reduction in patients compared to Pravachol.

114. At the time, Zocor (simvastatin) had FDA-approved indications for CV event reduction and a decrease in total mortality. BMS reps deliberately misled prescribers with this "Hydrophobic vs. Hydrophilic" statins article to lead them to believe that Pravachol was uniquely beneficial to patients while Zocor and other statins were actually harmful to patients. This was done by BMS to deliberately mislead doctors and to intend for doctors to submit false claims for payment to the Government.

115. An abstract was used by BMS in a slide deck entitled, "Pravastatin Turkish Trial (PTT): Study Design." This deck contained off-label and misleading information regarding other mechanisms, particularly as anti-thrombotic and anti-platelet mechanisms uniquely attributed to Pravachol, and was supplied to the MSAs, CMRS or Medical Science Liaisons (MSLs) and shared with the MSAs and/or CMRS reps. Slide 3 shows quotes that direct the provider to off-label and misleading "other mechanisms" as responsible for CV event reduction and states: "PTT: Early and combined use of pravastatin with thrombolytic therapy in AMI safely lowers lipid levels, decreases the incidence of major CV events. These benefits may result from direct reduction of cholesterol or a cholesterol independent effect of pravastatin on endothelial or platelet functions." In addition, Slide 16 points out additional off-label and misleading information that BMS was trying to present stating that allowing smooth muscle proliferation was a benefit of pravastatin versus other statins. Although the notes state that there is no definite link to differential